REMARKS

In the Office Action, the Examiner noted that: Claims 1-36 and 38-62 are pending the application, of which Claims 1-36 are withdrawn from consideration; Claims 38-54 and 57-62 are rejected; and Claims 55-56 are objected to. The claims have been amended and new claims added as noted above. Reexamination and reconsideration of the claims, as amended, are respectfully requested.

Response to Office Action Paragraphs 1-4

Claim Rejection Under 35 U.S.C. §112

In the Office Action the Examiner rejected Claims 60 and 61 under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner stated that "a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite ..." further indicating that "in the present instance, claim 62 recites the broad recitation "at least one other substance" and the claim also recites 'the at least one other substance is Methylprednisolone' which is the narrower statement of the range/limitation.

Given the above language and the reasoning given by the Examiner, Applicant's believe that the rejection was meant to be directed at Claim 61 (and 62 as a claim depending therefrom) and not 60 and 61.

By the present amendment, Applicants have amended Claim 61 to recite in part: "releasing mizoribine and methylprednisolone from the prosthesis when implanted in the blood vessel."

Applicants believe that this amendment obviates the rejection and respectfully request withdrawal of this rejection and the allowance of Claims 61 and all those depending directly or indirectly therefrom.

Response to Office Action Paragraphs 4-5

Claim Rejection Under Double Patenting

In the Office Action the Examiner provisionally rejected Claims 52-60 under the judicially created doctrine of obviousness-type double, over the copending Application No. 09/782,804.

Applicants respectfully acknowledge this rejection and will address this rejection once the claims are otherwise in condition for allowance.

Response to Office Action Paragraphs 6-7

Claim Rejection Under 35 U.S.C. §102(b)

In the Office Action the Examiner rejected Claims 38-54 and 57-60 under 35 U.S.C. §102(b) as being anticipated by Gregory et al. (USPN 5,283,257).

In rejecting the claims, Examiner noted that Gregory et al. discloses a method for treating hyperproliferative vascular disease by administering MPA (mycophenolic acid), and mizoribine as is claimed (referencing the abstract, column 3 lines 44-52, column 4 lines 17-31, column 6 lines 45-52, and column 12 lines 24-28 and 37-40).

Gregory et al. is directed to the use of MPA in preventing hyperproliferative vascular disease. Gregory et al. discloses in vivo and in vitro examples of the effect of administration of MPA, cyclosporine (CsA), FK 506, rapamycin (RPM), and MPA in combination with RPM on the intimal thickening. All of the limited examples in Gregory et al. were limited to systemic administration of the drugs. Although the description makes a reference to other ways for administering MPA, e.g., impregnation of a vascular stent with MPA, Gregory et al. provides no teaching or enablement whatsoever as to a method for inhibiting restenosis using mizoribine, and more particularly releasing mizoribine from a stent. The Gregory et al.references suffers from several problems:

Firstly, Gregory et al. at most provides a speculative reference as to the potential use of mizoribine.

Claims 52 and 60 as previously amended recite, in part: "... implanting a vascular prosthesis comprising a scaffold having means thereon for releasing mizoribine in the

blood vessel; and releasing mizoribine from the prosthesis into the blood vessel so as to inhibit smooth muscle cell proliferation."

In contrast to the present invention, Gregory et al. does not teach or suggest a prosthesis comprising a scaffold having means thereon for releasing mizoribine, as claimed in Claims 52 and 60.

Applicants submit that Claims 52 and 60 are not anticipated by or obvious in view of Gregory et al., and that they are patently distinguishable over the same. Applicants respectfully request the withdrawal of the rejection and request allowance of Claims 52 and 50 and all those Claims depending directly or indirectly therefrom.

Secondly, when Gregory does reference mizoribine, it is in combination with mycophenolic acid (in addition to the any such reference being vague). In rejecting the claims, Examiner refers to portions of the description which reference use of mizoribine in prevention of hyperproliferative vascular disease based on its classification as an IMP-DH inhibitor. However, the description, when in fact does mention mizoribine, it referes to the use of mizoribine in combination with MPA. Please see:

> Column 4 lines 17-23 stating "Other combinations containing mycophenolic acid that are useful for preventing or treating hyperproliferative vascular disease will be apparent to one skilled in the art. These include, but are not limited to, using mycophenolic acid in combination with other anti-proliferative antimetabolites or other drugs useful for the treatment of hyperproliferative diseases."
>
> Column 6 lines 59-63 stating "Accordingly, this result suggests that MPA, alone or in combination with other IMPH-DH inhibitors, may be particularly useful in treatment of intimal thickening when combined with other active agents."

Accordingly and more specifically, new Claim 63 recites in part: "implanting a vascular prosthesis comprising a scaffold having means thereon for releasing a therapeutic agent consisting essentially of mizoribine in the blood vessel."

Applicants submit that new Claim 63 is not anticipated by or obvious in view of Gregory, and that it is patently distinguishable over the same, and request allowance of the same.

Thirdly, Gregory only describes systemic administration of MPA and the other listed drugs, none of which includes mizoribine. The present claims are directed to local, not systemic, delivery of mizoribine.

Accordingly and more specifically, new Claim 64 recites in part: "implanting a vascular prosthesis comprising a scaffold having means thereon for releasing mizoribine to local area of treatment; and releasing mizoribine from the prosthesis to the local area of treatment so as to inhibit smooth muscle cell proliferation."

Applicants submit that new Claim 64 is not anticipated by or obvious in view of Gregory, and that it is patently distinguishable over the same, and request allowance of the same.

Fourthly, the described doses in Gregory (albeit only for MPA and some other agents none of which is mizoribine) are in amounts greater than those described and claimed in the present application in amounts greater than 10,000 fold. While Gregory describes using MPA at doses in the range of milligrams per kilogram per day, the present application (e.g., Claims 38 and 39) requires daily doses in the microgram range. That is, the daily dose in Gregory for an average patient having a weight of fifty (50) kilogram would be 2,000 milligrams (based on 40 miligrams of MPA/kg/day, see column 5 line 34) which is equivalent to 2,000,000 micrograms per day.

In contrast to Gregory, Claims 38 recites an upper range of about 200 microgram per day with Claim 39 having an upper range of 60 micrograms per day. The upper range of Claim 38 is thus smaller than that of Gregory by 10,000 fold.

Applicants respectfully submit that Claims 38 and 39 are not anticipated by or obvious in view of Gregory, and that they are patently distinguishable over the same, and request allowance of the same.

Information Disclosure Statement:

Applicants submit a PTO-1449 citing U.S. Patent No. 5,024,671, which was cited in a related PCT application. A copy of the Search Report is also included.

The Search Report was mailed on March 27, 2003, and Applicants believe that no fee is due. Should a fee be due, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to the above-noted Deposit Account.

Conclusion:

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

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